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(FILE 'USPAT' ENTERED AT 17:34:30 ON 14 JAN 97)

L1	1904 S (TUMOR NECROSIS FACTOR) OR TNF OR CACHECTIN
L2	251 S L1(P)RECEPTOR
L3	40 S L1(P)BINDING PROTEIN
L4	33 S L1(10A) ((BINDING PROTEIN) OR BP)
L5	157 S L1(P)INHIBITOR
L6	13 S L2(P)INHIBITOR

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1. 5,582,998, Dec. 10, 1996, Monoclonal antibodies against human **\*\*TNF\*\***-**\*\*binding\*\*** **\*\*protein\*\*** I (**\*\*TNF\*\***-**\*\*BP\*\*** I) and immunoassays therefor; G unther Adolf, 435/7.1, 7.92, 7.94, 70.21, 240.27; 436/811, 815; 530/388.1 [IMAGE AVAILABLE]
2. 5,525,626, Jun. 11, 1996, Treating susceptible human malignant tumors with 7-hydroxy-1,2-benzopyrone; Douglas R. Thornes, et al., 514/457; 424/649; 514/171, 274 [IMAGE AVAILABLE]
3. 5,519,119, May 21, 1996, Muteins of TNF pharmaceutical compositions and a method of making; Nobutoshi Yamada, et al., 530/351; 53/395, 402; 435/69.1, 69.5, 69.7, 252.3, 252.33, 320.1 [IMAGE AVAILABLE]
4. 5,512,544, Apr. 30, 1996, Pharmaceutical compositions comprising an anticytokine; David Wallach, et al., 514/12, 21; 530/350 [IMAGE AVAILABLE]
5. 5,478,925, Dec. 26, 1995, Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them; David Wallach, et al., 530/351; 424/85.1, 158.1, 450 [IMAGE AVAILABLE]
6. 5,476,774, Dec. 19, 1995, Quantitation of nucleic acids using the polymerase chain reaction; Alice M. Wang, et al., 435/91.2, 6, 320.1; 536/24.33; 935/77, 78 [IMAGE AVAILABLE]
7. 5,470,829, Nov. 28, 1995, Pharmaceutical preparation; Per Prisell, et al., 514/12; 424/85.1; 514/2, 8, 21; 525/54.1 [IMAGE AVAILABLE]
8. 5,464,820, Nov. 7, 1995, Specific inhibitors of tissue kallikrein; James Burton, et al., 514/16, 17, 18; 530/329, 331 [IMAGE AVAILABLE]
9. 5,426,181, Jun. 20, 1995, DNA encoding cytokine-induced protein, TSG-14; Tae H. Lee, et al., 536/23.5; 435/69.1, 252.3, 320.1; 536/23.1 [IMAGE AVAILABLE]
10. 5,395,760, Mar. 7, 1995, DNA encoding tumor necrosis factor-.alpha. and -.beta. receptors; Craig A. Smith, et al., 435/240.1; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 [IMAGE AVAILABLE] *Id May 10, 1990*
11. 5,359,039, Oct. 25, 1994, Isolated poxvirus A53R-equivalent tumor necrosis factor antagonists; Craig A. Smith, et al., 530/350; 424/186.1, 232.1; 530/826; 536/23.72; 930/220 [IMAGE AVAILABLE]
12. 5,359,037, Oct. 25, 1994, Antibodies to **\*\*TNF\*\*** **\*\*binding\*\*** **\*\*protein\*\*** I; David Wallach, et al., 530/388.22; 424/143.1, 172.1; 530/388.1, 389.1 [IMAGE AVAILABLE]
13. 5,344,915, Sep. 6, 1994, Proteins and the preparation thereof;

4 Hans-Georg LeMaire, et al., 530/350, 395, 413, 416 [IMAGE AVAILABLE]

14. 5,324,655, Jun. 28, 1994, Human Y-interferon signal peptide-tumor necrosis factor(TNF) gene fusions; Michael Kriegler, et al., 435/240.2, 69.1, 69.5, 69.7, 69.8, 172.1, 172.3, 240.1, 320.1; 536/23.1, 23.2, 23.4, 23.5, 23.52; 935/23, 24, 27, 32, 34, 44, 47, 48, 66, 70, 71 [IMAGE AVAILABLE]

15. 5,288,852, Feb. 22, 1994, Human tumor necrosis factor polypeptides; Masaaki Yamada, et al., 530/351; 424/85.1; 435/69.5, 69.7; 530/395; 930/144 [IMAGE AVAILABLE]

16. 5,262,309, Nov. 16, 1993, Terminal modifications of tumor necrosis factor; Satoshi Nakamura, et al., 435/69.5, 172.3; 530/351 [IMAGE AVAILABLE]

17. 5,256,568, Oct. 26, 1993, Vectors and transformed most cells for recombinant protein production with reduced expression of selectable markers; Nikos Panayotatos, 435/252.33, 69.1, 172.1, 172.3, 252.3, 320.1; 536/24.1 [IMAGE AVAILABLE]

18. 5,247,070, Sep. 21, 1993, N-terminal muteins of tumor necrosis factor; Nobutoshi Yamada, et al., 530/351; 424/85.1; 435/69.5, 69.7; 530/395, 402; 930/144 [IMAGE AVAILABLE]

19. 5,219,759, Jun. 15, 1993, Recombinant DNA encoding PDGF A-chain polypeptide and expression vectors; Carl-Henrik Heldin, et al., 435/320.1, 69.4; 530/324, 399; 536/23.5, 23.51 [IMAGE AVAILABLE]

20. 5,219,727, Jun. 15, 1993, Quantitation of nucleic acids using the polymerase chain reaction; Alice M. Wang, et al., 435/6, 91.2, 91.21; 536/24.33; 935/77, 78 [IMAGE AVAILABLE]

21. 5,182,196, Jan. 26, 1993, Expression systems for overproduction of desired proteins; Bernard Allet, et al., 435/69.5, 252.3; 536/23.5, 23.51 [IMAGE AVAILABLE]

22. 5,180,811, Jan. 19, 1993, Proteins having a TNF action comprising TNF-fibronectin fusion protein; Thomas Doerper, et al., 530/351; 424/85.1; 435/69.52, 69.7; 530/395; 930/144 [IMAGE AVAILABLE]

23. 5,151,349, Sep. 29, 1992, Method for expressing polypeptide having anti-tumor activity; Shoji Tanaka, et al., 435/69.1 [IMAGE AVAILABLE]

24. 5,147,638, Sep. 15, 1992, Inhibition of tumor growth by blockade of the protein C system; Charles T. Esmon, et al., 424/85.1, 85.2, 85.4, 85.5, 152.1, 172.1, 282.1; 435/212; 514/2, 8, 12; 530/351, 381, 388.25, 389.3 [IMAGE AVAILABLE]

25. 5,136,021, Aug. 4, 1992, TNF-inhibitory protein and a method of production; Wlodzimierz E. Dembinski, et al., 530/350, 351, 369 [IMAGE AVAILABLE]

26. 5,081,021, Jan. 14, 1992, DNA encoding HTNF variants exhibiting enhanced activity; Den'ichi Mizuno, et al., 435/69.5, 91.41, 320.1; 536/23.1, 23.5; 935/9, 11, 12, 13 [IMAGE AVAILABLE]

27. 5,043,271, Aug. 27, 1991, DNA encoding rabbit TNE, vector having said DNA inserted thereinto, host transformed with said vector, rabbit TNF polypeptide, and process for production thereof; Masaaki Yamada, et al., 435/69.5, 91.41, 172.3, 240.1, 240.2, 240.4, 252.3, 252.33, 320.1; 536/23.51, 24.1; 935/2, 11, 21, 27, 60, 73 [IMAGE AVAILABLE]

28. 5,028,420, Jul. 2, 1991, Muteins of tumor necrosis factor; Tsukio Masegi, et al., 424/85.1; 435/69.5, 320.1; 530/351 [IMAGE AVAILABLE]

29. 4,990,455, Feb. 5, 1991, Novel human TNF polypeptide mutants and DNA's encoding said mutants; Junichi Yamagishi, et al., 435/69.5, 69.1, 172.3, 252.3, 252.33, 320.1; 530/350, 351; 536/23.2, 23.5; 935/10 [IMAGE AVAILABLE]

30. 4,948,875, Aug. 14, 1990, Novel polypeptide having an anti-tumor activity and a method of preparation thereof; Shoji Tanaka, et al., 530/350; 435/69.1, 69.5; 530/351 [IMAGE AVAILABLE]

31. 4,880,915, Nov. 14, 1989, Method for purifying a physiologically active substance produced by recombinant DNA technique; Junichi Kajihara, et al., 530/413; 435/69.5; 530/350, 351, 415, 416, 828 [IMAGE AVAILABLE]

32. 4,879,226, Nov. 7, 1989, Novel human physiologically active polypeptide; Robert B. Wallace, et al., 435/68.1, 172.3, 240.2, 252.33, 254.2, 320.1, 948; 514/2, 12, 21; 530/350, 351, 828; 536/23.2, 23.5; 935/9, 11, 56, 73 [IMAGE AVAILABLE]

33. 4,650,674, Mar. 17, 1987, Synergistic cytotoxic composition; Bharat B. Aggarwal, et al., 424/85.5, 85.4; 435/69.5; 514/12; 930/143, 144 [IMAGE AVAILABLE]

1. 5,578,444, Nov. 26, 1996, Sequence-directed DNA-binding molecules compositions and methods; Cynthia A. Edwards, et al., 435/6, 7.23; 536/23.1; 935/76, 77 [IMAGE AVAILABLE]
2. 5,519,000, May 21, 1996, Tumor necrosis factor inhibitors; George A. Heavner, et al., 514/12, 13, 14, 15, 16, 17, 18; 530/324, 326, 328, 329, 330 [IMAGE AVAILABLE]
3. 5,506,340, Apr. 9, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]
4. 5,486,595, Jan. 23, 1996, Tumor necrosis factor inhibitors; George A. Heavner, 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]
5. 5,457,129, Oct. 10, 1995, Inhibition of nitric oxide production by retinoic acid; Bharat B. Aggarwal, et al., 514/557, 825, 895, 903 [IMAGE AVAILABLE]
6. 5,455,240, Oct. 3, 1995, Modulators of pneumococcal adhesion to cellular targets involving the platelet activating factor receptor, and uses thereof; Elaine I. Tuomanen, et al., 514/210; 424/122; 514/8, 25; 536/4.1, 17.4, 17.6, 21 [IMAGE AVAILABLE]
7. 5,451,518, Sep. 19, 1995, Purified human ceramide-activated protein kinase; Richard N. Kolesnick, 435/194; 424/94.5; 435/15 [IMAGE AVAILABLE]
8. 5,447,851, Sep. 5, 1995, DNA encoding a chimeric polypeptide comprising the extracellular domain of TNF receptor fused to IgG, vectors, and host cells; Bruce A. Beutler, et al., 435/69.7, 69.5, 240.2, 320.1; 530/300, 351; 536/23.4 [IMAGE AVAILABLE]
9. 5,422,120, Jun. 6, 1995, Heterovesicular liposomes; Sinil Kim, 424/450; 264/4.1, 4.3, 4.6; 436/829 [IMAGE AVAILABLE]
10. 5,227,368, Jul. 13, 1993, Endotoxin-induced thrombosis factor which induces procoagulant activity in endothelial cells; Herwig Gerlach, et al., 514/12; 530/324, 350, 351 [IMAGE AVAILABLE]
11. 5,225,212, Jul. 6, 1993, Microreservoir liposome composition and method; Francis J. Martin, et al., 424/450, 78.31, 426 [IMAGE AVAILABLE]
12. 5,136,021, Aug. 4, 1992, TNF-inhibitory protein and a method of production; Wlodzimierz E. Dembinski, et al., 530/350, 351, 369 [IMAGE AVAILABLE]
13. 5,071,872, Dec. 10, 1991, Method for improving interleukin-2 activity using aci-reductone compounds; Donald T. Witiak, et al., 514/473; 424/85.4, 85.7; 514/465, 889; 530/351 [IMAGE AVAILABLE]

AN - 91-081851/12  
 XRAM- C91-034797  
 TI - Insoluble tumour necrosis factor binding proteins - and DNA encoding them, useful in pharmaceutical prods. and for antibody prodn.  
 DC - B04 D16  
 PA - (HOFF ) HOFFMANN-LA ROCHE AG  
 IN - BROCKHAUS M,DEMBIC Z,GENTZ R,LESSLAUER W,LOTSCHER H,SCHLAEGER EJ NP - 1  
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 AB - (EP-417563)

Insoluble TNF-BPs, or soluble and insoluble fragments of these (55 or 75 kD SDS PAGE), in homogeneous form, and their salts are new. DNA sequence (I) encoding TNF-BPs, and derived amino acid sequences are given in the specification. (I) consists of a sequence encoding a TNF-BP and a sequence encoding all domains, except the first domain, of the human Ig having chain constant region (IgG, IgA, IgM, IgE, esp. IgM, IgG, type 1 or 3). TNF-BP can be prepared by culturing hosts, e.g. mammalian or insect cells, transformed with a vector containing (I), and isolating and purifying the product.

USE/ADVANTAGE - TNF-BP is used in a therapeutic product, and as a antigen for the production of mono- and polyclonal antibodies.

In an example specific TNF-binding capacity at various concns. is measured in a filter test:  $K_d = 10^{-9} - 10^{-10}$  M. (26pp Dwg.No.0/4)

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